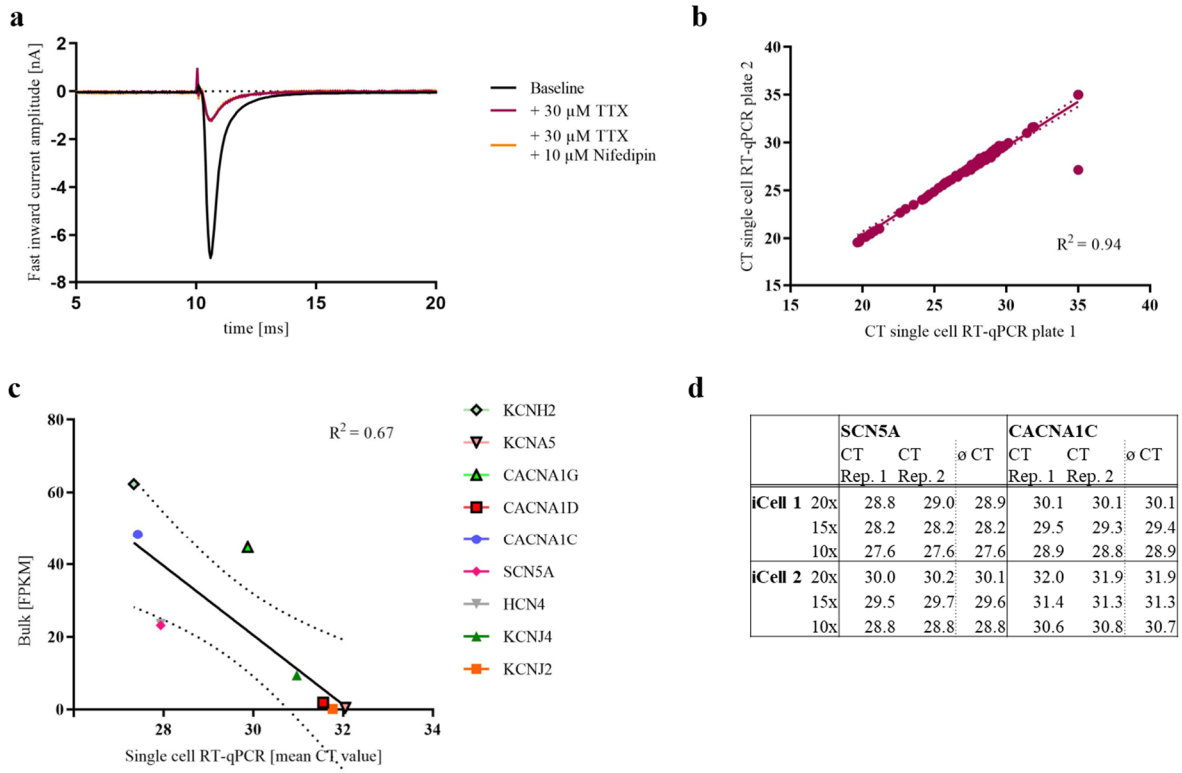
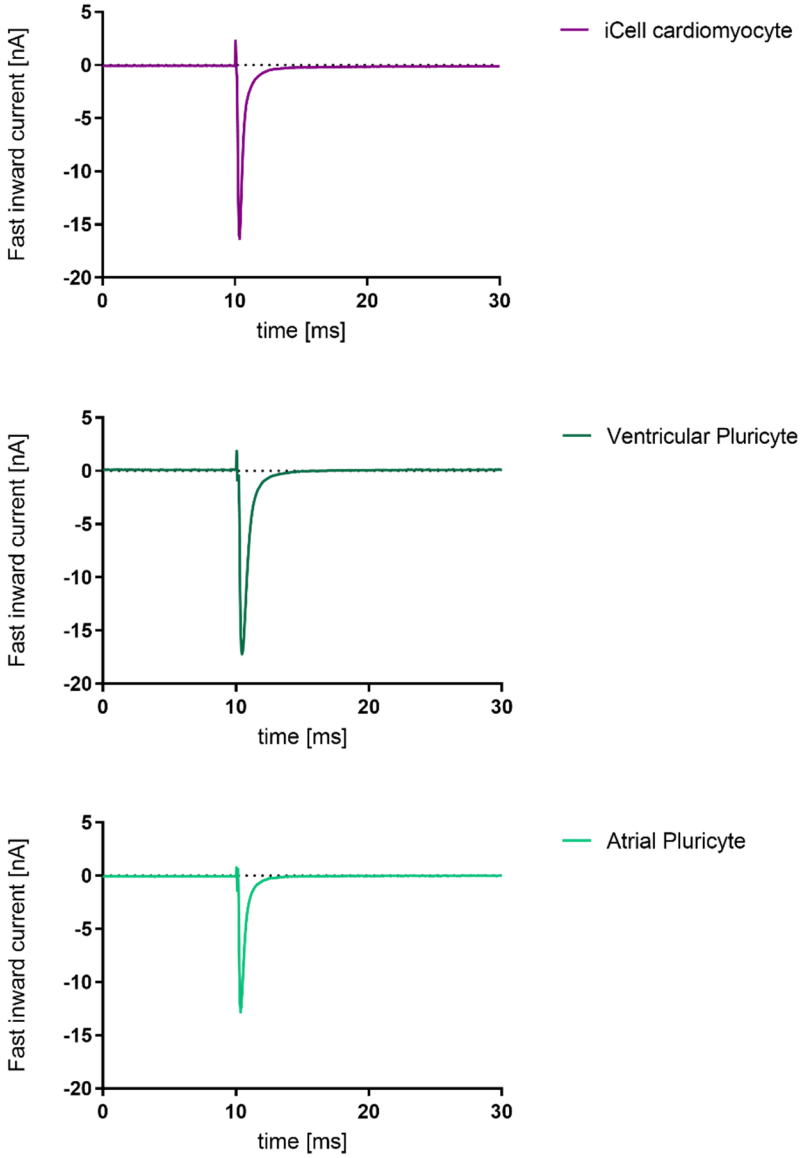
Supplementary information

Supplementary figures



		SCN5A			CACNA1C		
		CT Rep. 1	CT Rep. 2	ø CT	CT Rep. 1	CT Rep. 2	ø CT
iCell 1	20x	28.8	29.0	28.9	30.1	30.1	30.1
	15x	28.2	28.2	28.2	29.5	29.3	29.4
	10x	27.6	27.6	27.6	28.9	28.8	28.9
iCell 2	20x	30.0	30.2	30.1	32.0	31.9	31.9
	15x	29.5	29.7	29.6	31.4	31.3	31.3
	10x	28.8	28.8	28.8	30.6	30.8	30.7

Supplementary Figure S1: Reliability and reproducibility of experiments**.** All depicted validations have been performed using iCell cardiomyocytes. **(a)** Representative trace of the fast inward current. The current can be blocked with TTX, indicating the cardiac sodium channel $Na_V1.5$ (SCN5A) mainly conducts it. **(b)** The qPCR for different targets (HCN4, SCN5A, CACNA1C, KCNH2, TNNT2 and GAPDH) of 12 iCell cardiomyocytes was run twice on two different plates. CT values of both plates for each cell and target were plotted against each other. High correlation indicates low inter-plate variability. **(c)** Correlation of results of bulk sequencing (data were taken from [19]) and mean CT values of iCell cardiomyocytes. **(d)** Representative raw data results of qPCR of two iCell cardiomyocytes (iCell 1 and iCell 2) for SCN5A and CACNA1C. Note that dilutions of pre-amplified cDNA (10 – 15 -20x) reflect CT values (difference between 20x and 10x is one CT value) and that CT values of technical replicates are highly reproducible



Supplementary Figure S2: Representative fast inward current traces for iCell cardiomyocytes, ventricular Pluricytes, and atrial Pluricytes. To record the fast inward current, cells were clamped at a holding potential of -100 mV (to make sure sodium channels were not inactivated) followed by a voltage step to -30 mV for 100 ms. The numbers of total recordings are listed in Table 4.



Supplementary Figure S3: Binary expression of cardiac ion channels in single cardiomyocytes. Each row represents one cell. A green/red box indicates that the cell was positive/negative (for details see Methods section) for the respective ion channel.

Supplementary tables

Supplementary Table S1: Detailed information on donor hearts. In total four hearts were used. The number of cells per heart, tested in the current study, are listed. Abbreviations: F, Female; M, Male; BMI, Body Mass Index; COD, Cause Of Death; EF, Ejection Fraction; CVA, Cerebrovascular Accident; ICH, Intracranial Haemorrhage; [a]Organ procurement organization could not transplant the heart and consequently no echocardiography was performed; N/A, Not available.

Heart#	# of atrial cells	# of ventr. cells	Age	Sex	Ethnicity	BMI	COD	EF (%)
1	20	44	44	F	Hispanic	23.9	Anoxia	70
2	-	20	50	F	Caucasian	27.0	CVA/ICH/Stroke	70
3	1	26	48	M	Hispanic	29.7	CVA/ICH/Stroke	73
5	19	-	48	M	Caucasian	25.0	Head Trauma/Blunt Injury	N/A[a]

Supplementary Table S2: Single-cell correlations for iCell cardiomyocytes. For every pairwise correlation, Pearson´s correlation coefficient r, the p-value and *n* is indicated. For expression parameters (CT), only positive cells are included in the analysis. Significant correlations ($p < 0.05$) are highlighted.

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0
Number of Observations

	Capacitance [pF]	CT TNNT2	CT GAPDH	Beat rate [bpm]	Fast inward current amplitude [nA]	Fast inward current density [nA/pF]	CT KCNJ4	CT HCN4	CT SCN5A	CT CACNA1C	CT KCNH2	CT CACNA1D	CT CACNA1G	CT KCNA5	CT KCNJ2
Capacitance [pF]															
CT TNNT2	-0.47948 0.0002 55														
CT GAPDH	-0.41380 0.0019 54	0.63821 <.0001 54													
Beat rate [bpm]	0.39615 0.0006 72	-0.20614 0.1311 55	-0.09661 0.4871 54												
Fast inward current amplitude [nA]	-0.52661 <.0001 71	0.25793 0.0573 55	0.40036 0.0027 54	-0.32099 0.0063 71											
Fast inward current density [nA/pF]	0.22838 0.0554 71	-0.18581 0.1744 55	0.07108 0.6095 54	-0.04794 0.6914 71	0.57352 <.0001 71										
CT KCNJ4	-0.14583 0.3961 36	0.25792 0.1288 36	0.33011 0.0528 35	-0.03112 0.8570 36	0.06821 0.6926 36	-0.03945 0.8193 36									
CT HCN4	-0.13913 0.3110 55	0.57387 <.0001 55	0.62395 <.0001 54	-0.12547 0.3614 55	0.11026 0.4229 55	0.01460 0.9157 55	0.46450 0.0043 36								
CT SCN5A	-0.31477 0.0193 55	0.60979 <.0001 55	0.57934 <.0001 54	-0.22416 0.0999 55	0.33424 0.0126 55	0.12547 0.3614 55	0.28567 0.0912 36	0.63050 <.0001 55							
CT CACNA1C	-0.15034 0.2779 54	0.65659 <.0001 54	0.54573 <.0001 53	-0.05731 0.6806 54	0.13894 0.3164 54	-0.03184 0.8192 54	0.48559 0.0031 35	0.77101 <.0001 54	0.63570 <.0001 54						
CT KCNH2	-0.33075 0.0146 54	0.66434 <.0001 54	0.67170 <.0001 53	-0.27414 0.0449 54	0.24597 0.0730 54	-0.04697 0.7359 54	0.54151 0.0008 35	0.74212 <.0001 54	0.63704 <.0001 54	0.63982 <.0001 53					
CT CACNA1D	-0.51714 0.0402 16	0.21706 0.4194 16	0.35693 0.1747 16	-0.39439 0.1306 16	0.12324 0.6493 16	-0.30098 0.2573 16	0.26174 0.4112 12	0.38780 0.1378 16	0.27524 0.3022 16	0.20048 0.4566 16	0.45558 0.0879 15				
CT CACNA1G	-0.62623 0.0018 22	0.26047 0.2417 22	0.50993 0.0153 22	-0.52551 0.0120 22	0.30266 0.1710 22	-0.09500 0.6741 22	0.35683 0.1597 17	0.34438 0.1165 22	0.42360 0.0495 22	0.33256 0.1305 22	0.46296 0.0300 22	0.72164 0.0433 8			
CT KCNA5	0.20682 0.4422 16	0.43548 0.0918 16	0.24729 0.3558 16	-0.04316 0.8739 16	0.07185 0.7915 16	0.21550 0.4228 16	0.08566 0.8140 10	0.35294 0.1800 16	0.34730 0.1875 16	0.51606 0.0407 16	0.40845 0.1163 16	-0.75064 0.0519 7	-0.23409 0.6134 7		
CT KCNJ2	0.28982 0.2592 17	0.24953 0.3341 17	0.35331 0.1642 17	0.15514 0.5521 17	0.09899 0.7054 17	0.60831 0.0096 17	0.42002 0.1349 14	0.43623 0.0800 17	0.52937 0.0289 17	0.28982 0.2592 17	0.35981 0.1560 17	-0.09204 0.8004 10	-0.00349 0.9935 8	0.75423 0.0501 7	

Supplementary Table S3: Single-cell correlations for ventricular Pluricytes. For every pairwise correlation, Pearson´s correlation coefficient r, the p-value and *n* is indicated. For expression parameters (CT), only positive cells are included in the analysis. Significant correlations ($p < 0.05$) are highlighted.

Pearson Correlation Coefficients Prob > |r| under H0: Rho=0 Number of Observations								
	Capacitance [pF]	CT TNNT2	CT GAPDH	Beat rate [bpm]	Fast inward current amplitude [nA]	Fast inward current density [nA/pF]	Upstroke velocity [V/ms]	APD90 [ms]
Capacitance [pF]								
CT TNNT2	-0.47201 0.0097 29							
CT GAPDH	-0.56797 0.0013 29	0.72151 <.0001 29						
Beat rate [bpm]	0.25750 0.1548 32	0.22268 0.2456 29	0.14911 0.4401 29					
Fast inward current amplitude [nA]	-0.55135 0.0019 29	0.33893 0.0903 26	0.25595 0.2069 26	-0.28312 0.1367 29				
Fast inward current density [nA/pF]	0.38774 0.0377 29	-0.24292 0.2318 26	-0.40638 0.0394 26	-0.09831 0.6119 29	0.48312 0.0079 29			
Upstroke velocity [V/ms]	0.32201 0.0827 30	0.09515 0.6369 27	-0.05456 0.7869 27	0.44634 0.0134 30	-0.54228 0.0024 29	-0.39389 0.0345 29		
APD90 [ms]	0.14464 0.4296 32	-0.32318 0.0873 29	-0.33659 0.0742 29	-0.08132 0.6582 32	0.03141 0.8715 29	0.20910 0.2763 29	0.19974 0.2900 30	
CT KCNJ4	0.25169 0.3137 18	0.35900 0.1434 18	0.26974 0.2790 18	-0.17098 0.4975 18	0.18620 0.4899 16	0.30188 0.2558 16	-0.13674 0.6008 17	0.09025 0.7217 18
CT HCN4	-0.58489 0.0014 27	0.54664 0.0032 27	0.80464 <.0001 27	-0.09305 0.6443 27	0.28815 0.1721 24	-0.38461 0.0635 24	-0.08920 0.6716 25	-0.31381 0.1109 27
CT SCN5A	-0.54420 0.0023 29	0.73648 <.0001 29	0.66461 <.0001 29	-0.14862 0.4416 29	0.54891 0.0037 26	-0.04690 0.8200 26	-0.29704 0.1324 27	-0.17614 0.3607 29
CT CACNA1C	-0.26417 0.1661 29	0.70566 <.0001 29	0.78418 <.0001 29	0.17565 0.3621 29	0.11549 0.5742 26	-0.29148 0.1485 26	0.24990 0.2087 27	-0.28120 0.1395 29
CT KCNH2	-0.50268 0.0064 28	0.83824 <.0001 28	0.77068 <.0001 28	0.18654 0.3419 28	0.41888 0.0372 25	-0.07150 0.7341 25	-0.09468 0.6455 26	-0.28008 0.1489 28
CT CACNA1D	-0.60008 0.1543 7	0.13146 0.7787 7	0.50153 0.2515 7	-0.16058 0.7309 7	0.42476 0.3422 7	-0.00830 0.9859 7	-0.45459 0.3055 7	0.04534 0.9231 7
CT CACNA1G	-0.61184 0.1443 7	0.20023 0.6668 7	0.33206 0.4668 7	-0.26131 0.5714 7	0.89202 0.0069 7	0.47738 0.2787 7	-0.23095 0.6183 7	-0.62289 0.1351 7
CT KCNA5	0.05814 0.8504 13	0.05273 0.8642 13	0.15099 0.6224 13	0.38399 0.1952 13	-0.48551 0.0926 13	-0.55685 0.0481 13	0.51997 0.0685 13	-0.54486 0.0542 13
CT KCNJ2	-0.15219 0.4486 27	0.53316 0.0042 27	0.46542 0.0144 27	-0.08619 0.6691 27	0.08833 0.6746 25	-0.20747 0.3197 25	-0.09146 0.6568 26	-0.04127 0.8381 27

Supplementary Table S3 continued: Single-cell correlations for ventricular Pluricytes**.** For every pairwise correlation, Pearson´s correlation coefficient r, the p-value and *n* is indicated. For expression parameters (CT), only positive cells are included in the analysis. Significant correlations ($p < 0.05$) are highlighted.

Pearson Correlation Coefficients Prob > |r| under H0: Rho=0 Number of Observations									
	CT KCNJ4	CT HCN4	CT SCN5A	CT CACNA1C	CT KCNH2	CT CACNA1D	CT CACNA1G	CT KCNA5	CT KCNJ2
Capacitance [pF]									
CT TNNT2									
CT GAPDH									
Beat rate [bpm]									
Fast inward current amplitude [nA]									
Fast inward current density [nA/pF]									
Upstroke velocity [V/ms]									
APD90 [ms]									
CT KCNJ4									
CT HCN4	0.26439 0.3051 17								
CT SCN5A	0.31327 0.2056 18	0.58871 0.0012 27							
CT CACNA1C	0.39897 0.1010 18	0.69500 <.0001 27	0.65481 0.0001 29						
CT KCNH2	0.29053 0.2579 17	0.58006 0.0019 26	0.70330 <.0001 28	0.64720 0.0002 28					
CT CACNA1D	-0.72842 0.1006 6	0.10944 0.8153 7	0.71453 0.0712 7	0.34557 0.4477 7	0.38486 0.3939 7				
CT CACNA1G	-0.22706 0.6653 6	0.56515 0.1861 7	0.44023 0.3229 7	0.31254 0.4950 7	0.28417 0.5368 7	0.57174 0.4283 4			
CT KCNA5	-0.70958 0.0487 8	-0.00728 0.9830 11	-0.39804 0.1780 13	0.19096 0.5320 13	0.06333 0.8372 13	-0.97117 0.0288 4	-0.96253 0.0375 4		
CT KCNJ2	0.39873 0.1012 18	0.44569 0.0256 25	0.69364 <.0001 27	0.48381 0.0106 27	0.55861 0.0030 26	0.26194 0.5704 7	-0.53098 0.2201 7	-0.32365 0.2807 13	

Supplementary Table S4: Single-cell correlations for atrial Pluricytes. For every pairwise correlation, Pearson´s correlation coefficient r, the p-value and *n* is indicated. For expression parameters (CT), only positive cells are included in the analysis. Significant correlations ($p < 0.05$) are highlighted.

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0
Number of Observations

	Capacitance [pF]	CT TNNT2	CT GAPDH	Beat rate [bpm]	Fast inward current amplitude [nA]	Fast inward current density [nA/pF]	CT KCNJ4	CT HCN4	CT SCN5A	CT CACNA1C	CT KCNH2	CT CACNA1D	CT CACNA1G	CT KCNA5	CT KCNJ2
Capacitance [pF]															
CT TNNT2	-0.40012 0.0527 24														
CT GAPDH	-0.47483 0.0190 24	0.92612 <.0001 24													
Beat rate [bpm]	0.05421 0.7645 33	-0.34275 0.1011 24	-0.18465 0.3877 24												
Fast inward current amplitude [nA]	0.13761 0.4937 27	0.11004 0.6638 18	0.00055 0.9983 18	-0.14726 0.4636 27											
Fast inward current density [nA/pF]	0.44261 0.0208 27	-0.08424 0.7396 18	-0.23965 0.3382 18	0.02145 0.9154 27	0.87199 <.0001 27										
CT KCNJ4	0.04194 0.9084 10	0.41908 0.2280 10	0.38299 0.2747 10	-0.25614 0.4750 10	0.81202 0.0497 6	0.73600 0.0953 6									
CT HCN4	-0.26246 0.2153 24	0.83107 <.0001 24	0.82874 <.0001 24	-0.34095 0.1030 24	-0.02507 0.9213 18	-0.29049 0.2423 18	0.46375 0.1770 10								
CT SCN5A	-0.10878 0.6129 24	0.59705 0.0021 24	0.48698 0.0158 24	-0.42486 0.0385 24	0.58832 0.0102 18	0.36252 0.1393 18	0.22506 0.5319 10	0.63971 0.0008 24							
CT CACNA1C	0.01258 0.9557 22	0.74915 <.0001 22	0.62045 0.0021 22	-0.37129 0.0889 22	0.44823 0.0816 16	0.29919 0.2603 16	0.45614 0.1852 10	0.74993 <.0001 22	0.74429 <.0001 22						
CT KCNH2	-0.32193 0.1250 24	0.91934 <.0001 24	0.93871 <.0001 24	-0.26181 0.2165 24	0.20871 0.4059 18	-0.05058 0.8420 18	0.59746 0.0682 10	0.87736 <.0001 24	0.69341 0.0002 24	0.78575 <.0001 22					
CT CACNA1D	-0.02504 0.9267 16	0.24294 0.3646 16	0.29601 0.2656 16	-0.33018 0.2117 16	-0.35265 0.2609 12	-0.55552 0.0608 12	-0.26572 0.4895 9	0.54085 0.0305 16	0.22235 0.4078 16	0.21266 0.4291 16	0.33062 0.2110 16				
CT CACNA1G	-0.27952 0.3130 15	0.36712 0.1783 15	0.33911 0.2163 15	-0.50443 0.0552 15	0.08375 0.7958 12	-0.12437 0.7002 12	0.03913 0.9267 8	0.27949 0.3130 15	0.58176 0.0229 15	0.50953 0.0524 15	0.32717 0.2339 15	0.02963 0.9235 13			
CT KCNA5	-0.42523 0.0431 23	0.87963 <.0001 23	0.74687 <.0001 23	-0.28490 0.1876 23	0.05977 0.8137 18	-0.10873 0.6676 18	0.03325 0.9273 10	0.72943 <.0001 23	0.58483 0.0034 23	0.70372 0.0004 21	0.73649 <.0001 23	-0.13819 0.6098 16	0.48246 0.0685 15		
CT KCNJ2	-0.21663 0.4570 14	0.29410 0.3074 14	0.16978 0.5617 14	-0.53080 0.0508 14	0.35243 0.2878 11	0.09561 0.7798 11	-0.65207 0.1125 7	- 0.07961 0.7868 14	0.48736 0.0771 14	0.20556 0.5005 13	0.24389 0.4007 14	0.63635 0.0353 11	0.35503 0.2840 11	0.04165 0.8876 14	

Supplementary Table S5: Single-cell correlations for primary human ventricular cardiomyocytes**.** For every pairwise correlation, Pearson´s correlation coefficient r, the p-value and *n* is indicated. For expression parameters (CT), only positive cells are included in the analysis. Significant correlations ($p < 0.05$) are highlighted.

Pearson Correlation Coefficients Prob > |r| under H0: Rho=0 Number of Observations																
	Capacitance [pF]	CT TNNT2	CT GAPDH	Beat rate [bpm]	Fast inward current amplitude [nA]	Fast inward current density [nA/pF]	CT KCNJ4	CT HCN4	CT SCN5A	CT CACNA1C	CT KCNH2	CT CACNA1D	CT CACNA1G	CT KCNA5	CT KCNJ2
Capacitance [pF]															
CT TNNT2															
CT GAPDH		0.92943 <.0001 66													
Beat rate [bpm]															
Fast inward current amplitude [nA]															
Fast inward current density [nA/pF]															
CT KCNJ4		0.68812 <.0001 60	0.53555 <.0001 60												
CT HCN4		0.83212 <.0001 62	0.79769 <.0001 62				0.69715 <.0001 56								
CT SCN5A		0.93413 <.0001 66	0.86351 <.0001 66				0.70826 <.0001 60	0.83395 <.0001 62							
CT CACNA1C		0.85971 <.0001 66	0.83918 <.0001 66				0.50424 <.0001 60	0.78715 <.0001 62	0.89932 <.0001 66						
CT KCNH2		0.92163 <.0001 66	0.86418 <.0001 66				0.66709 <.0001 60	0.79228 <.0001 62	0.93961 <.0001 66	0.82845 <.0001 66					
CT CACNA1D		-0.50750 0.1631 9	-0.44537 0.2296 9				-0.55434 0.1214 9	- 0.90516 0.0051 7	-0.59789 0.0890 9	-0.68836 0.0404 9	-0.56775 0.1108 9				
CT CACNA1G		-0.38033 0.4570 6	-0.34388 0.5045 6				-0.19650 0.7090 6	- 0.51595 0.4841 4	-0.29833 0.5658 6	-0.36568 0.4759 6	-0.28523 0.5838 6	-1.00000 . 2			
CT KCNA5		0.66843 <.0001 58	0.55315 <.0001 58				0.49670 0.0001 55	0.53913 <.0001 54	0.69113 <.0001 58	0.59693 <.0001 58	0.72190 <.0001 58	-0.64581 0.0603 9	-0.40892 0.4208 6		
CT KCNJ2		0.91031 <.0001 64	0.89763 <.0001 64				0.54435 <.0001 59	0.77569 <.0001 60	0.91569 <.0001 64	0.88096 <.0001 64	0.86678 <.0001 64	-0.62797 0.0702 9	-0.16629 0.7529 6	0.53863 <.0001 57	

Supplementary Table S6: Single-cell correlations for primary human atrial cardiomyocytes. For every pairwise correlation, Pearson´s correlation coefficient r, the p-value and *n* is indicated. For expression parameters (CT), only positive cells are included in the analysis. Significant correlations ($p < 0.05$) are highlighted.

Pearson Correlation Coefficients
Prob > |r| under H0: Rho=0
Number of Observations

	Capacitance [pF]	CT TNNT2	CT GAPDH	Beat rate [bpm]	Fast inward current amplitude [nA]	Fast inward current density [nA/pF]	CT KCNJ4	CT HCN4	CT SCN5A	CT CACNA1C	CT KCNH2	CT CACNA1D	CT CACNA1G	CT KCNA5	CT KCNJ2
Capacitance [pF]															
CT TNNT2															
CT GAPDH		0.64314 <.0001 40													
Beat rate [bpm]															
Fast inward current amplitude [nA]															
Fast inward current density [nA/pF]															
CT KCNJ4		0.71803 <.0001 38	0.52165 0.0008 38												
CT HCN4		0.65271 <.0001 38	0.70499 <.0001 38				0.43418 0.0081 36								
CT SCN5A		0.92851 <.0001 40	0.65521 <.0001 40				0.77906 <.0001 38	0.63107 <.0001 38							
CT CACNA1C		0.75201 <.0001 39	0.79858 <.0001 39				0.74720 <.0001 37	0.62625 <.0001 37	0.82354 <.0001 39						
CT KCNH2		0.86837 <.0001 40	0.66604 <.0001 40				0.72826 <.0001 38	0.59691 <.0001 38	0.87227 <.0001 40	0.79846 <.0001 39					
CT CACNA1D		0.40383 0.0408 26	0.28054 0.1651 26				0.24616 0.2356 25	0.22168 0.2869 25	0.28739 0.1546 26	0.36581 0.0721 25	0.28597 0.1567 26				
CT CACNA1G		0.52913 0.0136 21	0.52760 0.0140 21				0.49896 0.0251 20	0.56495 0.0094 20	0.56293 0.0079 21	0.61373 0.0040 20	0.59517 0.0044 21	0.50094 0.0289 19			
CT KCNA5		0.79660 <.0001 40	0.71991 <.0001 40				0.67437 <.0001 38	0.60288 <.0001 38	0.74573 <.0001 40	0.80803 <.0001 39	0.68701 <.0001 40	0.44694 0.0221 26	0.58801 0.0051 21		
CT KCNJ2		0.52735 0.0019 32	0.65323 <.0001 32				0.37481 0.0345 32	0.38563 0.0322 31	0.57232 0.0006 32	0.61276 0.0002 31	0.56497 0.0008 32	0.30253 0.1712 22	0.78242 0.0001 18	0.58690 0.0004 32	

Supplementary Table S7: TaqMan gene expression assays used for experiments. Probes span introns whenever possible.

Gene (human)	# TaqMan assay
KCNJ2	Hs00265315_m1
KCNJ4	Hs00544821_m1
HCN4	Hs00175760_m1
SCN5A	Hs00165693_m1
CACNA1C	Hs00167681_m1
CACNA1D	Hs00167753_m1
CACNA1G	Hs00367969_m1
KCNA5	Hs00266898_s1
KCNH2	Hs00165120_m1
TNNT2	Hs00165960_m1
GAPDH	Hs00266705_g1